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# The Effect of Maternal Smoking on Placental Blood Flow Assessed Using IVIM

Devasuda Anblagan<sup>1</sup>, Nia W Jones<sup>2</sup>, Carolyn Costigan<sup>1</sup>, Ruta Deshpande<sup>2</sup>, Nick Raine-Fenning<sup>3</sup>, George Bugg<sup>2</sup>, Zdenka Pausova<sup>4,5</sup>, Tomáš Paus<sup>6,7</sup>, and Penny A Gowland<sup>1</sup>

<sup>1</sup>Sir Peter Mansfield Magnetic Resonance Centre, University of Nottingham, Nottingham, Nottinghamshire, United Kingdom, <sup>2</sup>Nottingham University Hospitals NHS Trust, Nottingham, Nottinghamshire, United Kingdom, <sup>3</sup>Division of Obstetrics & Gynaecology, School of Clinical Sciences, University of Nottingham, Nottingham, Nottinghamshire, United Kingdom, <sup>4</sup>Research Institute of the Hospital for Sick Children, University of Toronto, Toronto, Ontario, Canada, <sup>5</sup>Université de Montreal, Montreal, Quebec, Canada, <sup>6</sup>Rotman Research Institute, University of Toronto, Toronto, Ontario, Canada, <sup>7</sup>School of Psychology, University of Nottingham, Nottingham, Nottinghamshire, United Kingdom

**Introduction:** Uteroplacental and fetoplacental blood flows are essential requisites for successful fetal growth and development. High volume, low resistance blood flow in the placenta is thought to be essential for optimal materno-fetal nutrient exchange. Prenatal exposure to maternal cigarette smoking (PEMCS) is associated with increased risk of placental abruption, placenta praevia and intrauterine growth restriction<sup>1</sup>. In this study, we investigated changes in placental function in PEMCS using intravoxel incoherent motion (IVIM), a sensitive method of measuring blood movement, particularly in the placental intervillous spaces<sup>2</sup>.

**Aim:** To investigate the effect of PEMCS on placental blood flow.

**Methods:** Scanning: 18 pregnant women were recruited with local ethics committee approval: 10 smokers and 8 controls matched for age, parity, BMI, and education level. Pregnant women's self-reported smoking habits were recorded. All gave informed consent to participate in the study involving two scans at 22–27 weeks and 33–38 weeks gestational age (GA). Scanning was performed on a 1.5 T Philips Achieva MRI scanner with 5-element SENSE cardiac coil or 4-element SENSE torso coil, depending on the woman's size. Women lay on their right side in the decubitus position to avoid vena caval compression, and all these scans were conducted with a specific absorption rate of  $<2.0 \text{ W kg}^{-1}$ . The IVIM sequence used was a standard diffusion pulsed spin echo sequence acquired with 5 transverse slices encompassing the placenta in 108 seconds (TR = 3000 ms, TE = 95 ms, FOV =  $350 \times 350 \times 107 \text{ mm}^3$ ,  $1.46 \times 1.46 \times 7 \text{ mm}^3$ , 12 b values = 0, 1, 3, 15, 47, 80, 115, 206, 246, 346, 468 and  $800 \text{ s mm}^{-2}$ , repeated 5 times). Two controls were scanned with respiration-gating. Analysis: Regions of interest (ROI) comprising placenta, basal plate and chorionic plate were drawn around the whole placenta in a central slice for an intermediate b value. Each pixel in the ROI was fitted to the IVIM equation:  $S = S_0(1-f)e^{-bD} + fe^{-bD^*}$ , where  $S_0$  is the equilibrium signal,  $f$  is the moving blood volume of the placenta,  $D$  is the water self-diffusion coefficient and  $D^*$  is the pseudo diffusion coefficient. Data points corrupted by excessive motion were excluded and the data were refitted. The histogram for  $f$  and  $D$  in each ROI was found (skewed distribution). The mean, mode and fraction of pixels with  $f > 0.8$  ( $f_{hi}$ ) and  $D > 0.0025$  ( $D_{hi}$ ) in the histogram were found. The total placental volume was measured by drawing a mask around the placenta.

**Results:** Here, only results for mode  $f$  and mode  $D$  are quoted, although consistent trends were found for the mean,  $f_{hi}$  and  $D_{hi}$ . Note that the trends for mode  $f$  and mode  $D$  are the same in all directions for all areas. Figure 2 shows there was significant increase in mode  $f$  of the chorionic plate across gestation in both smoker ( $p > 0.05$ ) and control ( $p > 0.05$ ) group. Conversely, there was a significant decrease in the mode  $D$  of chorionic plate across gestation in both smoker ( $p < 0.01$ ) and control ( $p > 0.02$ ) group. A similar trend was observed in the basal plate region, although this was not statistically significant. However, mode  $f$  was significantly higher in the smoker group ( $p < 0.01$ ) at 22–27 weeks. Mode  $f$  and mode  $D$  for placenta are unchanged across gestation. Placental volume showed significant increase ( $p < 0.01$ ) across gestation but there was no significant difference between the two groups.

**Discussion:** Maternal smoking is associated with reduced total fetal volume and birth weight<sup>1,3</sup>. This study found an increase in moving blood volume ( $f$ ) in the basal plate of smokers at early gestation, which would be consistent with altered placental implantation, possibly related to the up-regulation of vascular growth factors by nicotine<sup>4</sup>. Subsequent reduction in blood flow may be due to impaired subsequent placental development; placental development is extremely sensitive to environmental impacts and the increased flow coupled with reduced arterial oxygenation due to carbon monoxide could lead to altered development. Considering changes with GA in both groups, constant flow in the placenta with GA suggests that the flow per unit volume of the growing placenta is unchanged during gestation, which is expected if it is optimized for maximal exchange. This would still be consistent with increased net exchange since the placenta grows with gestation, increasing the area for exchange. The decrease in  $D$  could be related to villous development. The reduction in  $D$  in the chorionic plate with GA suggests a change in tissue structure, which may relate to the need to provide mechanical support to the growing placenta, but could result from failures of the IVIM model coupled with increased flow to and from the placenta. **References:** [1] Persson P-H. (1978), Acta Obstetrica et Gynecologica Scandinavica. **57** (S78) 33-9. [2] R.J.Moore. (2000), Placenta, **21** 726-732. [3] D.Anblagan. Proc ISMRM 21 (2012). [4] F.Miceli. (2005) Biology of Reproductive **72** 628-632.

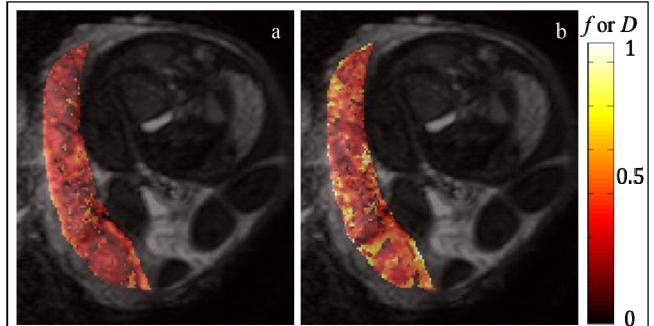


Figure 1: Map of  $f$ (a) and  $D$ (b) for a smoker subject at 34 weeks

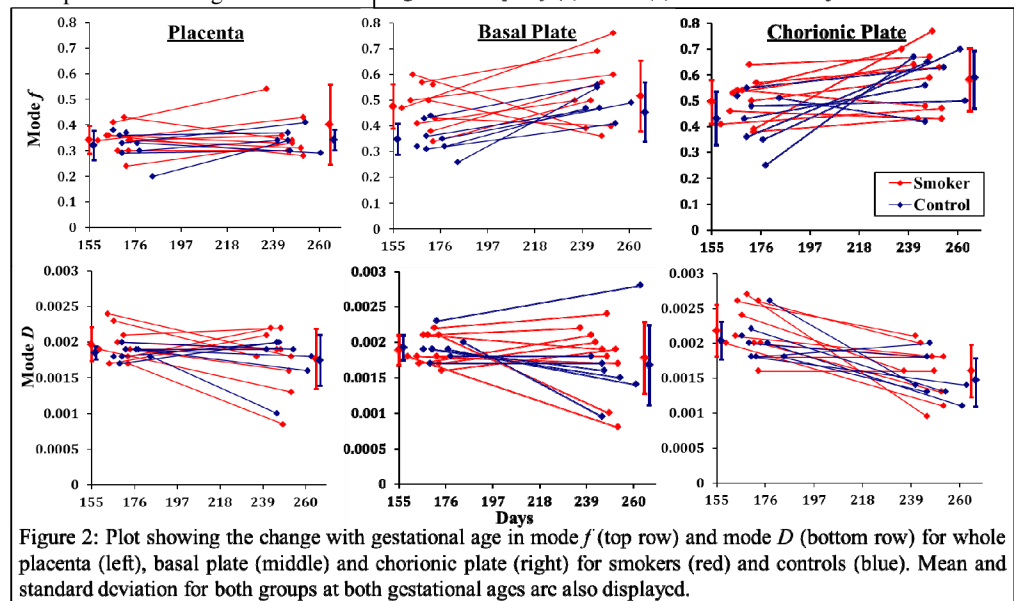


Figure 2: Plot showing the change with gestational age in mode  $f$  (top row) and mode  $D$  (bottom row) for whole placenta (left), basal plate (middle) and chorionic plate (right) for smokers (red) and controls (blue). Mean and standard deviation for both groups at both gestational ages are also displayed.